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Original Article

Leg movements and periodic leg movements during sleep in the development across childhood and adolescence from 1 to 18 years

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ABSTRACT

Objective: Age specific reference values of leg movements (LMS) and periodic leg movements (PLMS) in sleep considering their true periodicity to evaluate sleep pathologies, especially possible childhood RLS or PLMD.

Methods: In a prospective first night study of 52 healthy children/adolescents divided into six age groups from 1 to 18 years, polysomnographies were conducted and scored considering AASM rules. The frequency of LMS and PLMS were evaluated for NREM, REM, total sleep time (TST), including attention to time structure (inter-leg movement intervals, time distribution during the night) and periodicity of LMS.

Results: LMS and PLMS decreased with increasing age ($P < 0.05$). Children and adolescents older than 10 years had a PLMS index less than 5/h TST, in younger children the PLMS index was higher; 34.7% of total LMS and PLMS were accompanied by an EEG-arousal without age dependence. Periodicity index was low (median 0.2 decreasing with age to 0.1). Inter-leg movement intervals showed a decreasing incidence of shorter intervals with age. The course of LMS during the night displayed a lack of clear structure of distribution.

Conclusions: To evaluate pediatric motoric sleep disturbances it is necessary to consider the age dependence of LMS/PLMS and their true periodicity.

1. Introduction

Studies have demonstrated age dependence of the number of spontaneous leg movements in sleep (LMS) and especially of periodic leg movements in sleep (PLMS). Ferri et al. [1] have shown age-related changes in PLMS in patients with restless legs syndrome (range 7.5–83.2 years, mean 52.0), Pennestri et al. [2] in healthy subjects (range 5–76 years, mean 35.8), and Scholle et al. [3] described changing LMS in the age range 1–18 years. Marcus et al. [4] found no effect of age on the frequency of PLMS in the age range 5–17 years.

There are numerous articles describing LMS and PLMS in children and adolescents in connection with different sleep disturbances, for example restless legs syndrome (RLS), periodic leg movement disorder (PLMD) [5–11], narcolepsy [10,12–14], attention deficit/hyperactivity disorder (ADHD) [11,15–18], and obstructive sleep apnea [16,19–22], among others.

It has been shown that LMS constitute a specific marker for PLMD or RLS [5,6]. According to the American Academy of Sleep Medicine, five or more spontaneous stereotypical periodic limb movements per hour of sleep are defined as indicative of probable or possible PLMD and RLS in children aged 2–12 years [23].

Further understanding on how to differentiate and score movements in pediatric sleep is important for detecting disordered sleep. As described by Ferri et al. [24] there is ". . . a wide variety of different LM activities, ranging from the true periodic LM to isolated leg jerks or arousal-related irregular movements." Ferri et al. also suggested that ". . . a good synthesis of the features of LMS can be achieved by taking into account two main parameters: the total number of LMS per hour of sleep and their periodicity" [1]. PLMS index and periodicity index (PI) show different age-related changes and so the authors concluded that PLMS index and PI describe two distinct mechanisms.

The present study was designed to examine the age dependence of LMS and PLMS and to characterize the time structure and the true periodicity of these phenomena in healthy children and adolescents. Until now, such normative data in children and adolescents are missing [10]. In addition, we wished to address the question of whether the ICSD-2 criterion [23] regarding PLMS index is applicable for all age groups from 1 to 18 years of age. Determining age-related changes in LMS/PLMS index, time structure, and peri-

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odicity would be important to improve evaluation of pediatric sleep pathologies, especially possible childhood RLS or PLMD, as well as in evaluating other emerging conditions that exhibit a high prevalence rate of limb movements in sleep.

2. Methods

2.1. Subjects

One-night polysomnography was performed in a prospective study of 52 healthy German children of Caucasian ancestry (29 females, 23 males). These subjects were part of the normative study described by Scholle et al. [3,25,26].

Subjects were grouped by age. There were six groups aged from 1 to 18 years (median, 1.4, 3.5, 6.1, 12.0, 13.9, 17.3 years of age; Table 1). All investigated age groups consisted of carefully screened healthy subjects. Exclusion criteria included significant medical conditions and any indication of a sleep-related breathing disturbance or other sleep disorders. The body mass index of the subjects included was in the gender- and age-specific 5th–90th percentile range. No subject was using medications or supplements interfering with sleep. All subjects underwent a standard physical examination. Subjects were recruited for research purposes alone by means of advertisements in hospitals, neighboring nursery schools and other schools, and through families of hospital employees.

Children's habitual bedtimes were maintained. Written informed consents were obtained from the parents and children/adolescents. The local ethics committees approved the study.

2.2. Polysomnography

The examinations were conducted in accordance with American Academy of Sleep Medicine (AASM) rules for technical performance and scoring of sleep [27]. The Rembrandt polysomnography system (Embla Systems GmbH, Munich, Germany) was used. The following parameters were recorded: referential electroencephalogram (EEG) (F4M1, F3M2, C4M1, C3M2, O2M1, O1M2), submental surface electromyogram (EMG), referential electro-oculogram (E1M2 and E2M2), bipolar surface EMG from the right and left tibialis anterior muscle (separate channels), electrocardiogram (ECG), heart rate from ECG (R–R triggered), nasal pressure, rib cage and abdominal movements, oxygen saturation, snoring, body position, and digital video. Behavior was observed and recorded directly.

2.2.1. Analysis of polygraphic recordings

To exclude inter-scorer variability, polysomnography was scored by the same expert sleep researcher throughout the entire investigation. Sleep was staged in accordance with the AASM rules adapted for age [27].

Leg movements were scored when the duration was ≥0.5 and ≤10 s [28]. Movements >10 s up to <15 s without awakening were counted as movements with a length of 10 s. Longer movements ≥15 s were scored as movement times, reflecting the definitions of Rechtschaffen and Kales [29]. The minimum amplitude of a leg movement was an 8 μV increase in EMG voltage above the resting EMG. According to Zucconi et al. [28] and Iber et al. [27], onset was defined as the point at which there was an 8 μV increase in EMG voltage above resting EMG. The end of a leg movement was defined as the start of a period lasting ≥0.5 s during which the EMG did not exceed 2 μV above resting EMG. Leg movements that occurred during a period from 0.5 s preceding an apnea or hypopnea to 0.5 s following an apnea or hypopnea were not scored [27,28]. An arousal and a leg movement were considered to be associated with each other when there was <0.5 s between the end of one event and the onset of another, regardless of the order. Periodic leg movement series were defined as at least four consecutive leg movements, with a minimum period between leg movements of 5 s and a maximum period of 90 s [27,28]. For the evaluation of the periodicity index PI movements separated by an interval of >0.5 s were counted as two leg movements [9,10].

2.2.2. Parameters considered

The following parameters were considered in relation to age: (i) index of total LMS and PLMS, PLM index and index of isolated LMS per hour total sleep time (TST); (ii) index of total LM and PLM, PLM index and index of isolated LM per hour non-rapid eye movement (NREM) and rapid eye movement (REM) sleep; (iii) whether the movement occurred in the left or right side or bilaterally; (iv) all LMS and PLMS with cortical arousals (/h TST); (v) number of PLMS sequences and their duration; (vi) following time intervals between subsequent LMS [9,10]: interval 1 – onset to onset of two subsequent LMS (for the evaluation of the PI); interval 2 – offset to onset of two subsequent LMS (separation of different LMS, minimum 0.5 s); (vii) PI: number of sequences of at least three inter-LM intervals (10 s < i < 90 s) divided by the total number of inter-LM intervals (≥1 s) [9,10]; (viii) time distribution of total LMS including PLMS through the night.

The average LMS duration was not assessed because it has been reported that there is no difference between controls and patients [9].

2.3. Statistics

Statistical analyses were undertaken using Statistical Package StatView for Windows Version 4.57. As shown in [3], LMS and PLMS showed a skewed distribution. Therefore values are generally displayed as median and 10th and 90th percentile. Non-parametric statistical tests were preferred.

Differences between groups 1–6 were tested by Kruskal–Wallis *H*-test. Thereafter correlations between parameters and age were determined by Spearman's ρ. The number of inter-movement intervals in groups 1–3 versus 4–6 was assessed using the Mann–Whitney *U*-test. The dependency of PLMS index and periodicity index on age was tested by linear regression. $P < 0.05$ was considered significant.

3. Results

Age-dependent normative values of LMS and PLMS as well as PI and number of inter-LM intervals during TST, NREM, and REM are listed in Table 1.

The index of total LMS and PLMS decreased significantly with increasing age from 22.2/h TST [interquartile range (IQR) 12.8–27.2] in group 1 to 10.1/h TST (4.0–15.1) in group 6.

The index of total LMS and PLMS with cortical arousals decreased significantly with age from 5.7/h TST (4.7–8.5) in group 1 to 3.8/h TST (2.0–5.6) in group 6. Of all LMS and PLMS, 34.7% (24.3–55.8) were accompanied by an EEG arousal without age dependence.

The index of isolated LMS decreased significantly with age from 13.4/h TST (10.5–16.6) in group 1 to 7.8/h TST (4.0–12.8) in group 6. Of all movements, 70.5% (54.1–89.7) were isolated LMS without age dependence.

The incidence of total LM and PLM in NREM decreased significantly with age from group 1 [16.6/h NREM (10.4–21.3)] to group 6 [6.2/h NREM (2.6–11.7)]. Of all isolated LM, 47.2% (28.4–70.2) were bilateral movements; 25.2% (11.2–45.5) were registered on the right side and 23.0% (8.9–45.6) on the left side.

Total LM and PLM in REM decreased with age from 34.5/h REM (15.2–47.6) in group 1 to 21.7/h REM (9.1–35.7) in group 6. Of all isolated LM, 44.8% (25.6–66.1) were bilateral, 30.8% (13.1–48.6) monolateral right and 18.4% (5.6–42.4) monolateral left.

Table 1
Normative values of leg movements and periodic leg movements in sleep, related to age.

Variables	Group 1 ($n=9$)	Group 2 ($n=9$)	Group 3 ($n=9$)	Group 4 ($n=9$)	Group 5 ($n=8$)	Group 6 ($n=8$)	Group dependency *P*-value[a]	Age dependency *P*-value[b]
Age (years)	1.4 (1.0–2.2)	3.5 (2.8–4.7)	6.1 (4.9–10.0)	12.0 (11.7–13.0)	13.9 (13.4–15.0)	17.3 (16.8–17.9)		
Female/male	3/6	6/3	3/6	8/1	5/3	4/4		
TST (h)	8.8 (7.0–10.2)	9.2 (6.9–10.2)	9.2 (7.5–10.2)	8.6 (6.2–9.6)	8.5 (7.7–10.3)	8.5 (6.9–8.7)	NS	NS
NREM (h)	6.7 (5.1–7.2)	7.1 (5.3–7.7)	6.8 (6.2–7.9)	6.5 (5.0–7.5)	6.7 (5.9–7.8)	6.5 (5.5–7.1)	NS	<0.05
REM (h)	2.3 (1.5–3.1)	1.9 (1.4–2.6)	2.3 (1.3–2.6)	1.8 (1.1–2.5)	1.9 (1.6–2.6)	1.6 (1.3–2.5)	NS	NS
Total LMS and PLMS index (/h TST)	22.2 (12.8–27.2)	20.1 (11.2–25.4)	13.4 (9.6–23.0)	6.3 (4.1–18.8)	7.8 (3.8–13.6)	10.1 (4.0–15.1)	<0.05	<0.05
LMS and PLMS arousal index (/h TST)	5.7 (4.7–8.5)	6.1 (2.1–8.1)	5.0 (3.3–10.5)	3.6 (2.0–7.1)	2.6 (1.9–3.8)	3.8 (2.0–5.6)	<0.05	<0.05
Isolated LMS index (/h TST)	13.4 (10.5–16.6)	12.5 (8.5–15.7)	10.2 (5.8–12.7)	5.8 (3.2–12.2)	5.8 (3.2–8.5)	7.8 (4.0–12.8)	<0.05	<0.05
Bilateral (/h TST)	5.8 (3.8–8.6)	5.0 (3.4–6.4)	5.9 (2.8–8.1)	2.9 (1.8–8.2)	2.1 (1.3–3.6)	3.4 (1.8–5.4)	<0.05	<0.05
Monolateral right (/h TST)	3.6 (1.3–5.8)	2.7 (1.1–6.7)	2.9 (1.4–3.8)	1.6 (0.7–3.3)	1.8 (0.7–3.8)	2.4 (1.4–3.8)	NS	NS
Monolateral left (/h TST)	3.8 (1.7–7.7)	4.2 (2.4–5.6)	1.6 (1.1–3.2)	0.7 (0.2–3.2)	1.3 (0.3–2.8)	1.4 (0.4–4.1)	<0.05	<0.05
PLMS index (/h TST)	9.6 (2.0–10.9)	7.7 (2.9–10.8)	4.4 (1.7–10.4)	0.9 (0.4–6.6)	2.4 (0.5–6.2)	1.5 (0.0–4.7)	<0.05	<0.05
Bilateral (/h TST)	4.2 (1.1–5.3)	2.9 (0.7–5.2)	1.8 (1.0–5.8)	0.8 (0.1–4.8)	0.4 (0.0–1.9)	0.9 (0.0–2.7)	<0.05	<0.05
Monolateral right (/h TST)	1.2 (0.3–4.4)	1.2 (0.4–4.4)	1.3 (0.2–3.4)	0.1 (0.0–1.5)	0.7 (0.0–3.4)	0.4 (0.0–1.6)	NS	NS
Monolateral left (/h TST)	2.1 (0.3–4.3)	2.2 (0.8–4.7)	0.4 (0.1–2.4)	0.2 (0.0–0.9)	0.4 (0.0–3.2)	0.0 (0.0–0.7)	<0.05	<0.05
Number PLMS sequence	12.0 (3.4–19.6)	12.0 (3.8–17.0)	7.0 (3.8–12.2)	2.0 (1.0–11.6)	3.0 (1.0–8.8)	2.5 (0.0–7.2)	<0.05	<0.05
Duration PLMS sequence (s)	172 (138.1–199.6)	172.4 (133.9–199.6)	159.8 (126.6–240.8)	113.8 (69.0–184.3)	137.4 (78.0–383.1)	148.5 (94.3–260.4)	NS	NS
Periodicity index	0.2 (0.1–0.3)	0.1 (0.0–0.2)	0.2 (0.1–0.4)	0.1 (0.0–0.2)	0.2 (0.0–0.4)	0.1 (0.0–0.2)	<0.05	<0.05
Total LM and PLM index (/h NREM)	16.6 (10.4–21.3)	16.8 (9.9–27.1)	11.5 (7.6–23.0)	5.7 (2.2–18.9)	6.2 (2.8–16.0)	6.2 (2.6–11.7)	<0.05	<0.05
NREM LM and PLM index (/h TST)	12.3 (7.7–16.1)	13.1 (8.0–17.3)	8.6 (6.2–17.7)	4.6 (2.6–13.3)	4.9 (2.1–12.3)	4.9 (2.1–8.8)	<0.05	<0.05
Isolated LM index (/h NREM)	10.1 (8.1–13.8)	10.2 (6.9–17.9)	8.1 (4.4–11.1)	4.9 (2.6–10.4)	3.8 (2.0–9.6)	5.4 (2.7–10.5)	<0.05	<0.05
Bilateral (/h NREM)	4.8 (3.0–8.4)	4.2 (2.7–5.6)	5.0 (1.7–7.2)	2.8 (1.1–6.7)	1.4 (0.7–3.7)	2.1 (0.8–4.2)	<0.05	<0.05
Monolateral right (/h NREM)	2.0 (1.0–4.4)	2.2 (0.8–6.9)	2.0 (1.3–2.5)	1.5 (0.3–3.2)	0.8 (0.2–4.1)	1.5 (0.7–3.0)	NS	<0.05
Monolateral left (/h NREM)	2.9 (1.1–5.3)	3.2 (1.8–4.4)	1.6 (0.9–2.4)	0.6 (0.2–2.9)	1.2 (0.3–3.3)	1.0 (0.3–4.1)	<0.05	<0.05
PLM index (/h NREM)	6.1 (1.5–9.9)	6.9 (2.5–9.6)	4.6 (1.0–12.0)	1.2 (0.2–7.2)	1.8 (0.6–8.3)	0.0 (0.0–2.2)	<0.05	<0.05
NREM PLM index (/h TST)	4.5 (1.1–7.3	5.1 (2.0–7.4)	3.3 (0.4–10.0)	0.9 (0.2–5.5)	1.4 (0.4–6.2)	0.0 (0.0–1.6)	<0.05	<0.05
Bilateral (/h NREM)	2.0 (0.5–4.4)	3.0 (0.8–5.0)	1.9 (0.5–6.6)	1.1 (0.1–5.0)	0.4 (0.1–2.2)	0.0 (0.0–1.3)	<0.05	<0.05
Monolateral right (/h NREM)	1.2 (0.1–3.8)	1.3 (0.2–3.3)	1.5 (0.2–3.7)	0.2 (0.0–1.8)	0.4 (0.0–4.4)	0.0 (0.0–0.6)	<0.05	<0.05
Monolateral left (/h NREM)	1.6 (0.3–3.7)	1.2 (0.7–5.2)	0.3 (0.0–2.9)	0.2 (0.0–1.0)	0.5 (0.0–4.2)	0.0 (0.0–0.5)	<0.05	<0.05
Total LM and PLM index (/h REM)	34.5 (15.2–47.6)	30.9 (16.6–42.8)	17.9 (13.2–28.0)	13.5 (1.7–22.7)	7.4 (4.3–20.9)	21.7 (9.1–35.7)	<0.05	<0.05
REM LM and PLM index (/h TST)	9.6 (3.1–6.5)	7.1 (3.1–8.8)	4.9 (2.7–8.1)	2.1 (0.4–5.3)	1.6 (0.8–5.3)	5.1 (1.5–7.1)	<0.05	<0.05
Isolated LM index (/h REM)	21.2 (14.9–27.3)	19.8 (14.9–26.5)	15.6 (11.5–23.1)	13.5 (1.7–19.2)	7.5 (4.3–15.1)	13.3 (9.1–23.5)	<0.05	<0.05
Bilateral (/h REM)	8.3 (4.9–10.5)	9.0 (4.9–10.4)	8.3 (5.6–12.9)	4.3 (1.1–13.0)	2.4 (1.3–6.1)	5.8 (3.9–12.0)	<0.05	<0.05
Monolateral right (/h REM)	5.3 (1.9–10.4)	4.3 (1.9–8.3)	5.1 (1.8–7.5)	3.2 (0.2–4.6)	3.1 (2.3–7.0)	5.6 (3.5–8.2)	NS	NS
Monolateral left (/h REM)	6.5 (3.2–14.2)	6.2 (4.6–12.3)	2.2 (0.3–6.7)	1.1 (0.2–5.7)	1.0 (0.0–3.1)	2.0 (0.8–7.4)	<0.05	<0.05
PLM index (/h REM)	13.1 (0.2–22.4)	6.2 (1.5–18.1)	3.7 (0.2–6.3)	0.0 (0.0–4.1)	0.0 (0.0–5.8)	4.4 (0.0–20.1)	<0.05	<0.05
REM PLM index (/h TST)	2.9 (0.1–6.5)	1.6 (0.3–3.9)	0.9 (0.5–1.7)	0.0 (0.0–1.0)	0.0 (0.0–1.4)	1.1 (0.0–3.5)	<0.05	<0.05
Bilateral (/h REM)	4.3 (0.0–11.1)	1.7 (0.0–7.2)	1.1 (0.2–3.7)	0.0 (0.0–3.7)	0.0 (0.0–2.9)	3.1 (0.0–10.5)	<0.05	<0.05
Monolateral right (/h REM)	3.6 (0.0–7.7)	1.2 (0.0–7.9)	0.7 (0.0–2.2)	0.0 (0.0–0.5)	0.0 (0.0–2.5)	1.1 (0.0–7.9)	<0.05	NS
Monolateral left (/h REM)	2.5 (0.2–10.4)	3.5 (0.0–6.7)	0.5 (0.0–2.7)	0.0 (0.0–1.3)	0.0 (0.0–0.4)	0.0 (0.0–3.1)	<0.05	<0.05

Abbreviations: TST, total sleep time; NREM, non-rapid eye movement sleep; REM, rapid eye movement sleep; LMS, leg movements during sleep; PLMS, periodic leg movements during sleep; LM, leg movement; PLM, periodic leg movement; NS, non-significant.
Data are presented as median (10th–90th percentile).
[a] Kruskal–Wallis *H*-test.
[b] Spearman ρ-correlation.

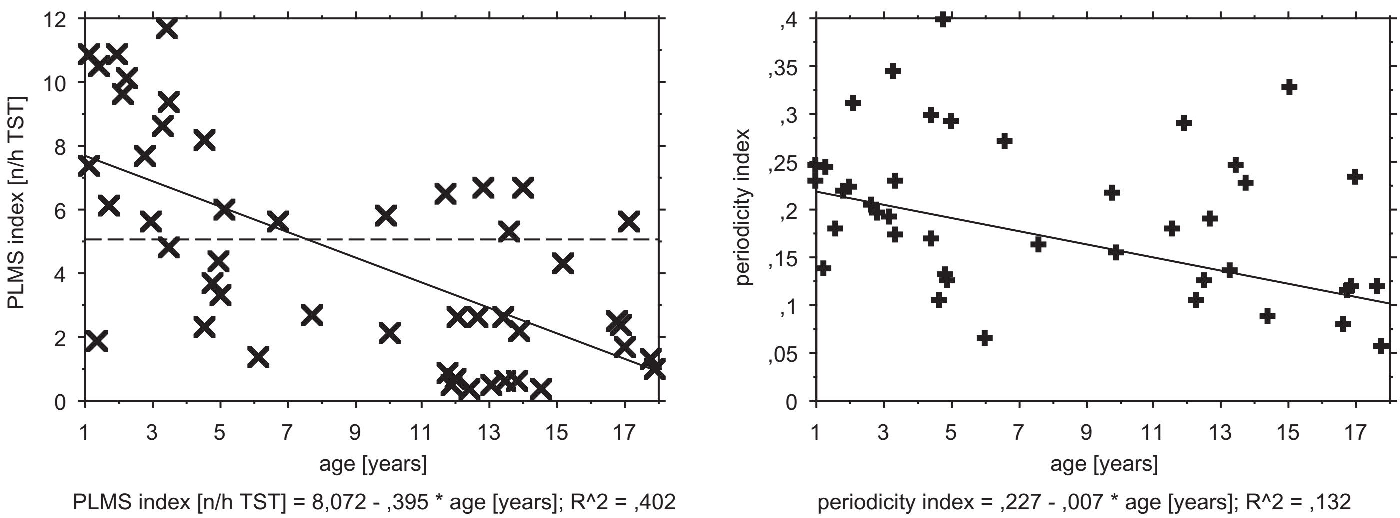

Fig. 1. Evolution of periodic leg movements in sleep (PLMS) index and periodicity index (PI) in the age range from 1 to 18 years of age: results of the linear regression analysis. The PLMS index, illustrated by the horizontal dashed line at $n = 5$, should invoke the guideline: "≥5 PLMS/h TST are indicative for possible childhood RLS [restless leg syndrome]" [23].

In NREM there were fewer total LM and PLM than in REM (NREM/REM ratio 61.3% (25.3–96.3). This ratio was not age dependent.

Fig. 1 shows PLMS index and periodicity index in dependence of age. The PLMS index decreased significantly from 9.6/h TST (2.0–10.9) in group 1 to 1.5/h TST (0.0–4.7) in group 6 (Fig. 1). PI decreased significantly from 0.2 (0.1–0.3) in group 1 to 0.1 (0.0–0.2) in group 6. This low incidence reflects the low real periodicity of leg movements in healthy children and adolescents.

Fig. 2 shows distribution histograms of the inter-LM intervals during sleep in the six different age groups. The incidence of intervals 0.5–10 s is high, especially in groups 1–3, decreasing and reaching a regular level at around 40 s. The course of the histograms is significantly different in groups 1–3 versus groups 4–6. Only intervals with a length of 17, 33, 43, 63, 69, 79, 85, 89, 93, 95, and 97 s do not show significant difference (*U*-test, $P > 0.05$).

Fig. 3 shows the course of LMS during the night in the six different age groups from 1 to 18 years, which displayed a lack of clear structure of distribution of LMS per hour of sleep. In the last third of the night, there is a slight increase in the number of leg movements, possibly in concert with more REM sleep.

4. Discussion

The study presents reference values showing age dependence of the number of isolated LMS and especially PLMS in healthy children and adolescents. To characterize disturbances of sleep caused by leg movements it is necessary to know the density of these movements in healthy children [11].

4.1. *Age dependence of PLMS index during childhood and adolescence*

There are several publications on PLMS in children. As in adults, four or more consecutive leg movements are needed to define a periodic leg movement series [27,28]. Five or more PLMS per hour sleep are defined as diagnostic criteria for RLS and PLMD in children aged 2–12 years [8,11,23,30]. In the literature, a 5–25% prevalence rate of ≥5 PLMS/h TST in children referred for sleep studies was reported [15,16,19].

As Ferri [31] outlined, the value of the PLMS is influenced by the number of LMS. As shown in our study, leg movements in the first years of life are frequent. The number of short intervals between LMS is higher in younger children (groups 1–3) than in older children and adolescents (groups 4–6) (Fig. 2). Because leg movements in the younger groups were on average more closely spaced, more movements fulfilled the criterion: time between leg movements is 5–90 s involving a minimum of four consecutive movements in periodic leg series movements [27,28]. As shown in Table 1, the 90th percentile of PLMS from 10 years onward is around 5/h TST (see also Fig. 1). But younger children aged 1–9 years have more PLMS considering the scoring criteria of Zucconi et al. [28], Iber et al. [27] and Picchietti et al. [8]. So for children aged ≤9 years it seems that the critical value to define a pathological density of PLMS should be corrected.

In the first years of life in children, a lot of leg movements are normal, decreasing with increasing age (Table 1). On average, 34.7% (24.3–55.8%) of all LMS and PLMS are accompanied by cortical arousals without age dependence (Table 1). Kirk and Bohn [16] found only 1% PLMS associated with arousals. They explained this very low incidence by pointing to problems with the arousal definition. In our study, we considered the AASM definition [27].

Especially in older children and adolescents aged ≥10 years, the PLMS index is low and the index of total LMS and PLMS is lower than in younger children (Table 1). Picchietti et al. [32] calculated in 10 control children, mean age 11.1 years (range 9.9–12.7), a PLMS index of 2.0 (0–4.9/h TST), comparable with our results. Pennestri et al. [2] reported a mean PLMS index of 4.8/h in children aged 5–9 years ($n = 7$) and 3.3 in children aged 10–19 years ($n = 9$). This is congruent with our results. Marcus et al. [4] described no age dependence of PLMS in the age range 5–17 years with a median PLMI of 0/h, ranging from 0 to 35.5/h. As shown in Fig. 1, the decline in the number of PLMS is most evident at age 1–5 years, which may explain the finding by Marcus et al. [4].

The frequency of LMS and PLMS in groups 3 and 4 of our study is comparable with the frequency reported by Ferri et al. [18] for controls aged 7–12 years and the number of PLMS sequences is comparable for each given age. The number of PLMS sequences in our study decreased with age from 12.0/TST (3.4–19.6) in the first age group to 2.5/TST (0.0–7.2) in group 6.

The duration of PLMS sequences (Table 1) in our study is longer than that reported by Ferri et al. [18]. For the estimation we included only polysomnographies with PLMS sequences. Hence the difference from the results of Ferri et al. [18] may arise from different methods of statistical analyses.

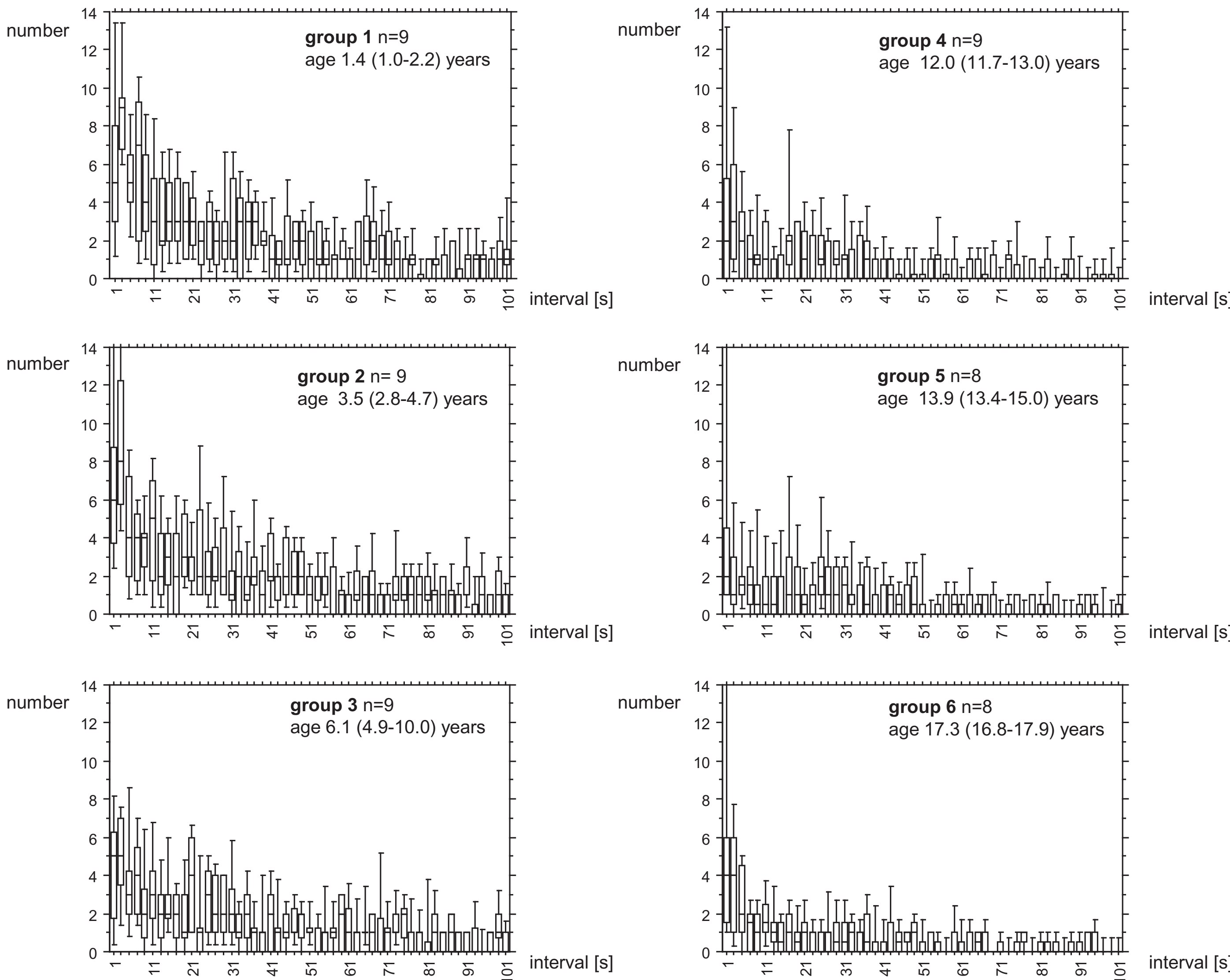

Fig. 2. Distribution histograms of the inter-leg-movement intervals during sleep in different age groups. Values are shown as boxplots (median and 10th, 25th, 75th and 90th percentiles).

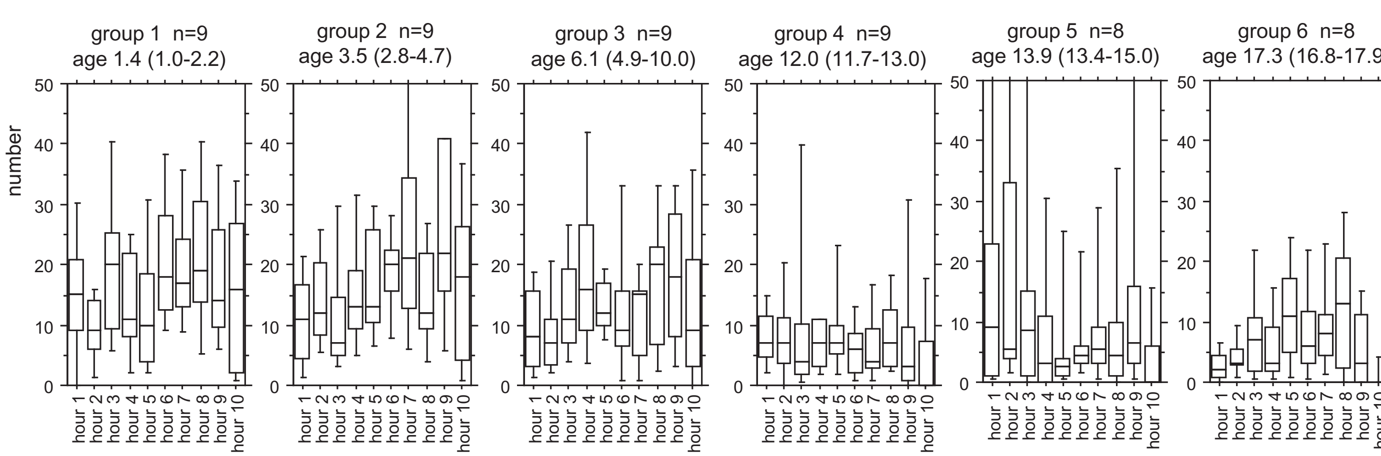

Fig. 3. Distribution of number of total leg movements in sleep (isolated and periodic limb movements) per hour of sleep in age groups 1–6.

Peirano et al. [33] examined LMS activity parameters in controls aged 10 years. The number of total LM and PLM, PLM index and isolated LM index is comparable with our results in group 3 (Table 1) for total sleep and NREM sleep, but in REM sleep we have found more isolated LM and therefore more total LM and PLM but a comparable number of PLM.

The decreasing number of total leg movements (isolated and periodic) in childhood may be explained by the maturation of the motoric system. In middle-aged and older subjects, leg movements increase, as shown by Ferri [1], Pennestri [2] and co-investigators. Pennestri et al. [2] suggested that this increase “is probably associated with the decrease of D_2 receptors, which is observed in healthy humans and animals with advancing age.”

4.2. LM/PLM index in REM and NREM sleep

Especially in the youngest children aged <5 years in this study (Table 1), there were a lot of leg movements both in REM and NREM. Twitches in the muscles of extremities decreased significantly in REM as well as in NREM with increasing age (Table 1).

Khatwa and Kothare [34] noted that PLM are reduced or absent in REM. Vetrivelan et al. [35] concluded that REM sleep is characterized by “. . . a complete muscle atonia in the somatic musculature except the ocular and inner ear muscles and diaphragm.” However, brief twitches in both cranial and spinal musculature are typical for REM.

This study has shown – surprisingly – that there is approximately double the rate of leg movements per hour REM compared with NREM. There were no changes in the ratio of leg movements per hour REM and per hour NREM in the age range from 1 to 18 years. In accordance with our results in adults, Ferri et al. [10] recorded more LM in REM (10.0 ± 7.1) than in NREM (7.5 ± 4.7). In children aged 7–12 years Ferri [31], determined a total index of leg movements in REM of 11.9 ± 5.7 and NREM of 11.3 ± 5.2. This frequency of occurrence is comparable with our results if we calculate the total index of REM-LM per hour TST (Table 1). Related to TST in REM, there were fewer LM and PLM than in NREM. This may be explained by the shorter duration of REM in the TST.

Sleep polygraphic studies of children and adolescents with narcolepsy/cataplexy have shown that, especially in REM sleep, narcoleptic patients show significantly more periodic or isolated LM in comparison with age- and sex-matched controls [12]. This confirms the need to evaluate the rate of LM according to sleep stages.

4.3. Inter-LM intervals in healthy children/adolescents

As outlined by Ferri et al. [24] there are limitations to using the PLMS index diagnostically as defined by the AASM definitions [27]. A new periodicity index [9,10] and the distribution of inter-LM intervals would better describe the time structure of leg movement activity during sleep. Pichietti et al. [8] pointed out the need to research the periodicity of PLMS in children. As shown by Ferri et al. [1,18] inter-LM intervals in children are short and variable in contrast to adults. Pennestri et al. [2] had declared that 15–35 s intervals in adults are typical whereas PLMS do not show a preferential interval in healthy children and adolescents. They concluded “. . . that interval evaluation is an important feature of the calculation of periodic movements to discriminate spontaneous motor activity from PLMS.” Histograms of the inter-LM intervals as shown by Pennestri et al. [2] for those aged 5–9 and 10–19 years are comparable with our results (Fig. 2).

In our results the distribution of inter-LM intervals in healthy children/adolescents shows a decreasing incidence of shorter intervals with age (Fig. 2). We found that by comparison with adults [8,9] the variability of the number of inter-LM intervals of different duration was very high, especially in the younger children. Furthermore, the incidence of intervals 0.5–10 s was high, especially in groups 1–3, decreasing and reaching a regular level at around 40 s. Comparing children aged 1–10 years (groups 1–3) with children/adolescents aged 11–18 years (groups 4–6) the distribution of inter-LM-intervals was significantly different (Fig. 2) with more intervals in the first age groups. The distribution of inter-LM intervals corresponds with distribution histograms shown by Ferri [31] for controls aged 7–12 years. They observed in adults [9] a maximum value for short intervals of 0.5–2 s and a rapid decrease to 8–10 s. In our study, there was a greater number of shorter intervals, from 0.5 to 20 s in children compared with adults.

4.4. Age dependence of the periodicity index

Ferri et al. [9,10] defined a new periodicity index (PI) with the intention to better characterize the real periodicity of leg movements. Fig. 1 shows the PLMS index and the PI with respect to age from 1 to 18 years. More LMS in younger children were reflected by a higher PLMS index. As Ferri [31] outlined, “. . . the value of the PLMS index is evidently influenced by the number of LMS and, to a lesser extent, by the real periodicity of the phenomenon.” At a significance level of $P < 0.05$ we see an age dependence of the PI from 0.2 (0.1–0.3) in group 1 to 0.1 (0.0–0.2) in group 6. The PI is around 0.2 for the whole of childhood and adolescence, reflecting the low real periodicity of leg movements in childhood and adolescence. This is a real advantage for the characterization of pathologies such as narcolepsy, restless legs syndrome, ADHD, obstructive sleep apnea, and others associated with increased leg movements. Thus the PI should provide a reliable means to assess leg movements in diagnosing sleep disorders and other associated pathologies.

4.5. Distribution of the number of LM activities during the night

Ferri et al. [10] reported a decline in PLMS from the beginning to the end of sleep in RLS patients aged 15–75 years [1]. In our study, we did not observe such a decline in LMS in the six age groups during the course of the night (Fig. 3). This may show that PLMS in healthy children/adolescents is dissimilar to dopamine-responsive PLMS occurring in RLS of adults.

4.6. Limitations of the study

This study included only Caucasian German subjects. Therefore the data may not be directly applicable to other racial/ethnic groups. O'Brien et al. [36] and Gingras et al. [22] had shown that PLMS are significantly more prevalent among Caucasian children than African-American children.

Another limitation was that this study was conducted during a single night. This is important because the night-to-night variability of periodic leg movements has been described, with more frequent LMS occurring in the first night [37–40]. However, in the clinical setting, two-night polysomnographic investigations are seldom possible and therefore first-night data are helpful. On the other hand, Ferri et al. [40] had shown a lower night-to-night variability in the PI.

5. Conclusions

Summarizing the polysomnographic findings of LMS/PLMS in healthy children/adolescents, it is necessary to consider the age dependency of LMS, with an enhanced frequency of limb movements in younger children. In young children up to 10 years of age, a PLMS index >5/h TST is normal.

For the detection of motoric sleep disturbances in childhood, it is necessary to describe the real periodicity of leg movements in-

cluding the PI, the inter-LM intervals and the time distribution during the night. The combination of PLMS index and periodicity index should be used together in studies on PLMS. In this way, the published normative values for children and adolescents in different age groups may be helpful.

Conflict of interest

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.04.018.

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